Symptomatic Management of MS:

Invisible Symptoms

MS Symptom Overview

- Fatigue (most common)
- Loss of sensation
- Decreased visual acuity, diplopia
- Pain
- Sexual dysfunction
- Paresthesias
- Emotional disturbances
- Cognitive difficulties (memory, attention, processing)
- Heat sensitivity
- Spasticity
- Gait, balance, and coordination problems
- Speech/swallowing problems
- Tremor
- Weakness
- Bladder and/or bowel dysfunction

Halper J, Harris C. Nursing Practice in Multiple Sclerosis: A Core Curriculum. 3rd ed. New York: Springer Publishing Company, 2012.

FATIGUE

Fatigue

"a subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities"

Multiple Sclerosis Council for Clinical Practice Guidelines, Paralyzed Veterans of America. *Fatigue and Multiple Sclerosis. Evidence-Based Management Strategies for Fatigue in Multiple Sclerosis.* Washington, DC: Paralyzed Veterans of America; 1998.

Fatigue

- The most common and disabling symptom of MS[1,3]
- Experienced by up to 95% of patients[2]
- 50-60% describe it as on of their most troubling symptoms[2]
- Reported in all disease stages and subtypes[2]
- Some evidence that lesions in the basal ganglia and hypothalamus may play an important role[2]

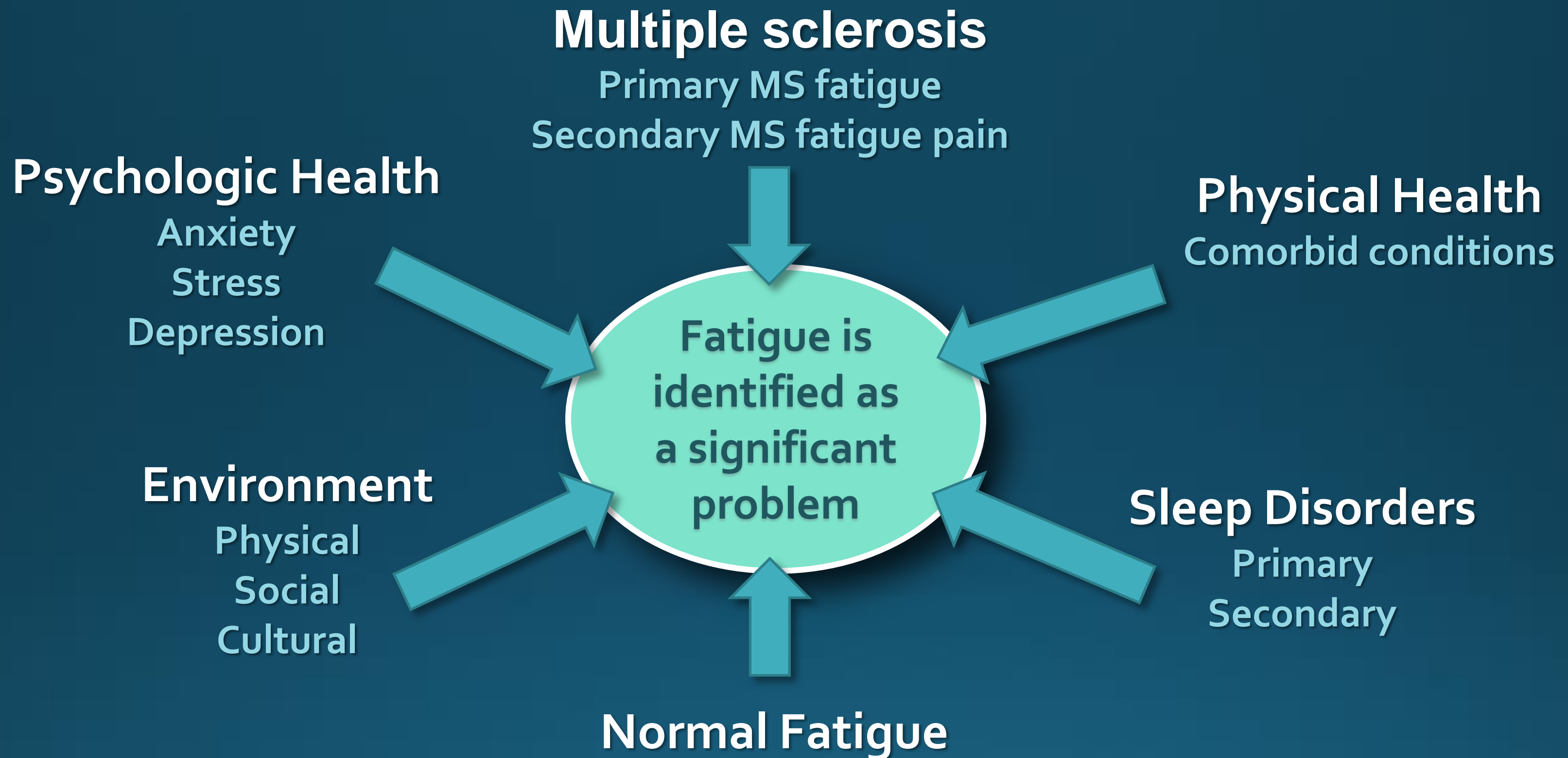
1. Schapiro. Managing the Symptoms of Multiple Sclerosis. (6th ed). New York: Demos Medical Publishing, 2014.
2. Amato, Portaccio. *Expert Opin Pharmacother*. 2012 Feb;13(2):207-216.
3. Halper, Harris. Nursing Practice in MS: A Core Curriculum. 3rd ed. NY: Springer Publishing, 2012.

Clinical Characteristics of Fatigue

- Overwhelming sense of sleepiness
- Constant sense of tiredness
- Lack of energy
- Feeling of exhaustion
- Not necessarily related to level of disability
- May affect motor function
- May affect cognitive function
- Not fully understood

Comi G, Leocani L. *Expert Rev Neurother*. 2002;2:867-876.
Krupp LB. *CNS Drugs*. 2003;17:225-234.
Multiple Sclerosis Council for Clinical Practice Guidelines. *Fatigue and MS: Evidence-Based Management Strategies for Fatigue in Multiple Sclerosis*. 1998.

Potential Causes and Effects



Krupp. Fatigue in MS. *CNS Drugs*. 2003;17:225-234; MS Council for Clinical Practice Guidelines. *Fatigue and MS: Evidence-Based Management Strategies,* 1998; Kos et al. *Neurorehabil Neural Repair.* 2008 Jan–Feb; 22(1): 91–100. Walters, Mulroy. *Gait Posture*. 1999; 9: 207–231 Sandroff et al. *J Neurol Sci*. 2013; 328(1–2): 70–76; Garrett, Coote. *Phys Ther Rev.* 2009;14(3):169–180; White, Castellano. *Sports Med.* 2008;38(2):91–100; Motl et al. *Mult Scler*. 2005;11(4):459–463.

Assessment Tools

- Fatigue Severity Scale
- Fatigue Impact Scale
- Modified Impact Scale
- Fatigue Descriptive Scale
- Fatigue Scale for Motor and Cognitive Functions

Amato, Portaccio. *Expert Opin.Pharmachother*. 2012;13(2):207-216.
Bennett et al. *Int J MS Care*. 2014; 16(Suppl 1):25-32.

Fatigue Management

- Exercise
- Address secondary causes
- Cooling techniques
- OT/PT: energy conservation techniques
- Pacing
- Stress management

Amato, Portaccio. *Expert Opin.Pharmachother*. 2012;13(2):207-216.
Bennett et al. *Int J MS Care*. 2014; 16(Suppl 1):25-32.

Pharmacologic Treatment

Drug	Dose	Adverse Effect
Amantadine	100-200 mg/d	Hallucinations Livido reticularis Nausea Lightheadedness Insomnia Constipation
Modafinil	Up to 400 mg/d	Headache Nausea Rhinitis Insomnia

Rosenberg JH, Shafor R. *Curr Neurol Neurosci Rep*. 2005;5(2):140-146.

Rammohan KW, Lynn DJ. *Neurology*. 2005;65(12):1995-1997.

Harris C, Halper J, eds. *Multiple Sclerosis: Best Practices in Nursing Care—Disease Management, Pharmacologic Treatment, Nursing Research.* 3rd ed. Hackensack, NJ:IOMSN; 2010.

Pharmacologic Treatment (cont.)

Drug	Dose	Adverse Effect
Methylphenidate	10-60 mg/d	Nausea Lightheadedness Insomnia Constipation Hypertension Tachycardia
Dextroamphetamine	5-40 mg/d	Nausea Feeling faint Insomnia Constipation Hypertension Tachycardia

Krupp, Christodoulou. *Curr Neuro Neurosci Rep*. 2001;1(3):294-298. Olson, et al. *Psychosomatics.* 2003;44(1):38-43. Medline Plus Drug Information: Methylphenidate: http://www.nlm.nih.gov/medlineplus/druginfo/meds/a682188.html.
Medline Plus Drug Information: Dextroamphetamine
http://www.nlm.nih.gov/medlineplus/druginfo/meds/a605027.html.

Patient Resources

- Multiple Sclerosis Foundation. Fighting Fatigue. http://www.msfocus.org/article-details.aspx?articleID=48.
- National MS Society. Fatigue: What you should know. A guide for people with MS. http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-Fatigue-What-You-Should-Know.pdf

COGNITION

Cognition and MS

- Cognitive impairment may be detected in 20-30% of patients at the time of first diagnosis[1,2]
- 40-65% will demonstrate cognitive dysfunction at some point in their illness[1,3]
- 10-15% will experience decreased job performance or altered social skills[3]
- Prevalence increases with age and duration of MS[1,2]

1. Freedman, et al. *Can J Neurol Sci* . 2013;40:307-323.
2. Benedict, Zivadinov. *Nat Rev Neuroll*. 2011;7:332-342.
3. Schapiro. Managing the Symptoms of MS. (6th ed). New York: Demos Medical Publishing, 2014.

Characteristics of MS-related Cognitive Dysfunction

- Does not correlate with physical disability
- May be subtle
- May be under-recognized or denied by patient, family, friends, or employers
- Deficits are not diffuse or global such as seen in Alzheimer's Disease

Crayton et al. *Neurology.* 2004;63(11 Suppl 5):S12-S18.
Foley et al. *Int J MS Care*. 2014; 16(Suppl 1):33-36.

Risk Factors

- Early age of onset
- Male sex[1]
- Gray matter atrophy
- Secondary Progressive Course[1]
- Low average or inferior intelligence
- Smoking[1]
- Inhaled cannabis?[1]

1. Benedict, Zivadinov. *Nat Rev Neurol* 2011;7:332-342.

Prevalence by Cognitive Domain

Domains	
Memory	30%
Information processing	25%
Problem solving	20%
Visuospatial abilities	20%
Attention/concentration	10%
Verbal fluency	10%

One domain: 50% Multiple domains: 22%

LaRocca. In: Multiple Sclerosis Diagnosis, Medical Management, and Rehabilitation. 2000:405-409.

Screening Tools for Cognitive Impairment

- **Symbol Digits Modalities Test (SDMT)**
  - Most reliable and valid psychometric measure of neuropsychological status
  - In brain imaging research, SDMT has often been the most robust cognitive correlate of brain pathology
- **California Verbal Learning Test-II (CVLT-II)**
  - Abbreviated version of CVLT-II captures 96% of variance in predicting memory impairment in MS

Benedict, Zivadinov. *Nat Rev Neurol* 2011:7:332-342.
Morrow et al. *J Neurol.* 2011; 258(9): 1603–1608.
Gromisch et al. *Mult Scler*. 2013; 19(4): 498–501.
Foley et al. *Int J MS Care*. 2014; 16(Suppl 1):33-36.

Further Cognitive Evaluation

- Neuropsychological testing may include: Rao Brief Repeatable Neuropsychological Battery, Minimal Assessment of Cognitive Function in MS, and the Brief International Cognitive Assessment for MS
- Practical applications
- Supports employment, legal cases
- Clarifies that problems do or do not exist
- Performed by a neuropsychologist, occupational therapist, or speech/language pathologist

Crayton et al. *Neurology.* 2004;63(11 Suppl 5):S12-S18.
Foley et al. *Int J MS Care*. 2014; 16(Suppl 1):33-36.

Managing Cognitive Impairment: Non-pharmacologic Treatment

- Discuss the problem openly; include family or significant other
- Counseling or psychotherapy
- Cognitive rehabilitation for coping and "compensatory strategies"
- Physical and/or occupational therapy for safety strategies and environmental modifications

Foley et al. Int J MS Care. 2014; 16(Suppl 1):33-36.

Managing Cognitive Impairment: Pharmacologic Treatment

- Disease-modifying therapies to slow disease progression
- Medications to slow cognitive dysfunction or help prevent progression have not been shown to be effective for MS

Foley et al. Int J MS Care. 2014; 16(Suppl 1):33-36.

Patient Resources

- Multiple Sclerosis Foundation. Cognitive Deficits in Multiple Sclerosis. http://www.msfocus.org/article-details.aspx?articleID=46.
- National MS Society. Solving Cognitive Problems: Managing Specific Issues. http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-Solving-Cognitive-Problems.pdf

PAIN

Acute Pain

Acute Pain is the normal, predicted physiological response to a noxious chemical, thermal, or mechanical stimulus and typically is associated with invasive procedures, trauma, and disease. It is generally time-limited.

(North Carolina Board of Medicine)

Chronic Pain (Non-malignant)

Generally considered to be pain that lasts more than 6 months, is ongoing, is due to non-life threatening causes, has not responded to current available treatment methods, and may continue for the remainder of the person's life.

(American Pain Society)

Pain Types

- **Nociceptive Pain**
  - Result of stimulation of nociceptors that signal tissue irritation or injury to elicit appropriate response. Typically described as aching and/or throbbing.
- **Neuropathic Pain**
  - Result of injury or malfunction of the peripheral or central nervous system. Described as lancing, pins and needles, burning electric shock.

Solaro, Uccelli. *Nature Reviews.* 2011;7: 519-527.

Pain and Multiple Sclerosis

- Pain prevalence reports vary from 29-86% of MS patients [1,2]
- More than 50% MS patients find pain to be a problem, and for 10-20% it is a significant problem.[3]
- Pain is estimated to comprise nearly 30% of all symptomatic treatment.[4]
- Under recognized and often inadequately managed.[5]
- Manageable in most patients.[5]

1. Solaro et al. *Neurology.* 2004;63:919-921.
2. Beiske et al. *European Journal of Neurology.* 2004;11:479-482.
3. Schapiro. Managing the Symptoms of MS. (6th ed). New York: Demos Medical Publishing, 2014.
4. Solaro, Uccelli. *Nature Reviews.* 2011;7:519-527.
5. Hoffman KJ. *Way Ahead.* 2005;9(1):8-9.

Pain Risk Factors

- Older age
- Longer disease duration
- Greater disease severity
- Men and women are equally likely to experience pain, but women tend to have greater severity of pain
- Progressive forms of MS
- Co-morbid depression and mental health impairment

O'Connor et al. Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain* 2008;137:96-111.

Pain Subtypes Common in MS

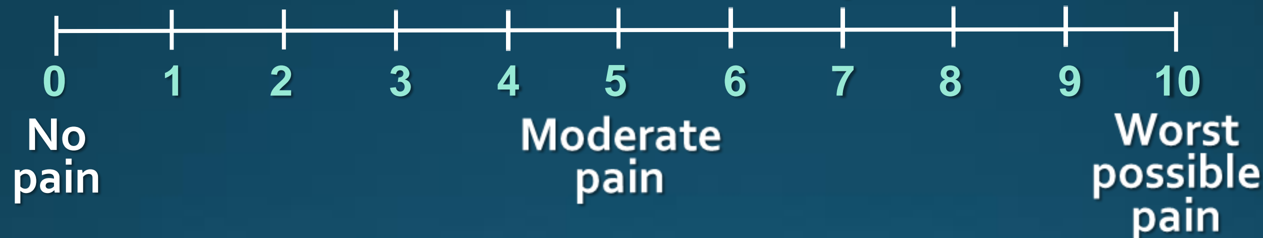
- **Continuous Central Neuropathic Pain**
  - (example: dysesthetic extremity pain)
- **Intermittent Central Neuropathic Pain**
  - (example: trigeminal neuralgia, Lhermitte's sign, painful tonic spasms)
- **Musculoskeletal Pain**
- **Mixed Neuropathic and Non-neuropathic Pain**
  - (example: headaches)

O'Connor et al. *Pain* 2008;137:96-111.
Maloni.http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf.
Solaro, Uccelli. *Nat Rev Neurol.* 2011 Aug 16;7(9):519-27.

Visual Analog Scale

Simple Descriptive Pain Intensity Scale[1]

0 – 10 Numeric Pain Intensity Scale[1]



Visual Analog Scale (VAS)[2]

[1] If used as a graphic rating scale, a 10 cm baseline is recommended.
[2] A 10 cm baseline is recommended for VAS scales.

Burckhardt, Jones. *Arthritis Rheum* 2003;49:S96–104.

Pharmacologic Treatment

Drug	Dose	Adverse Effect
Gabapentin	100-3600 mg/d	Fatigue Somnolence Dizziness Ataxia
Carbamazepine	400-1000 mg/d	Dizziness Drowsiness Nausea Unsteadiness
Amitriptyline	10-150 mg/d	Drowsiness Dry mouth Fatigue Constipation

Schapiro. *Neurorehabil Neural Repair*. 2002;16(3):223-231.
Solaro, Uccelli. *Nat Rev Neurol*. 2011; 7(9): 519–527.

Pharmacologic Treatment (cont.)

Drug	Dose	Adverse Effect
Misoprostol	100-200 mg/qid	Diarrhea Abdominal pain Nausea Dyspepsia
Topiramate	25-400 mg/d	Fatigue Somnolence Cognitive dysfunction Weight loss

Schapiro. *Neurorehabil Neural Repair*. 2002;16(3):223-231.
Kline et al. *South Med J*. 2003;96:602-605.

Pharmacologic Treatment (cont.)

Drug	Dose	Adverse Effect
Pregabalin	150-600 mg/d	Dry mouth Constipation Unsteadiness Somnolence
Duloxetine	60-120 mg/d	Upset stomach Vomiting Constipation Dizziness

MedlinePlus. Pregabalin http://www.nlm.nih.gov/medlineplus/druginfo/meds/a605045.html.
MedlinePlus. Duloxetine http://www.nlm.nih.gov/medlineplus/druginfo/meds/a604030.html.

Non-pharmacologic Treatment Measures

- Stretching for spasticity
- Massage
- Distraction
- Acupressure and Acupuncture
- Cooling
- Guided imagery
- Chronic Pain Management Program
- Physical and occupational therapy

Archibald CJ, et al. *Pain*. 1994;58(1):89-93.
Bashir K, Whitaker JN. *Handbook of Multiple Sclerosis*. 2002

Patient Resources

- National MS Society. Pain: The Basic Facts. Multiple Sclerosis. http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-Pain-The-Basic-Facts.pdf

DEPRESSION

Depression

A common mental disorder characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration.

(World Health Organization)

Depression in MS

- Up to 50% lifetime risk for Major Depressive Disorder (MDD) in the MS population [1,2]
- Incidence of depression is three times greater than the general population.[2]
- Etiology is unknown (related to MS pathophysiology, meds used to treat MS, or the challenges of living with MS) [3]
- Presence of depressive symptoms does not correlate well with the severity of disability [1, 2]
- Suicide has been indicated as cause of death for up to 15% of MS patients [1]

1. Goldman Consensus Group. *Multiple Sclerosis 2005;* 11: 328-337.
2. Paparrigopoulos et al. *International Review of Psychiatry* 2010;22(1):14-21.
3. Crayton et al. *Neurology.* 2004;63(11 Suppl 5):S12-S18.

Depression in MS

- Weak association may exist between depression and disease-modifying therapies [1]
- Fatigue, psychomotor retardation, poor concentration, sleep and appetite disturbances overlap both MDD and MS [2,3]
- MDD continues to be under- diagnosed and under-treated [2,4]

1. Crayton et al. *Neurology.* 2004;63(11 Suppl 5):S12-S18.
2. Paparrigopoulos et al. *International Review of Psychiatry* 2010;22(1): 14-21.
3. Goldman Consensus Group. *Multiple Sclerosis 2005;*11:328-337.
4. Majmudar, Schiffer. *Int J MS Care* 2009;11:154-159.

Screening for Depression

- Most commonly used: Beck Depression Inventory scale, with a cutoff score of 13 [1]
- Beck Depression Inventory – Fast Screen [1]
- Other options: Depression Scale (CES-D), Chicago Multi-Scale Depression Inventory, [1] and Beck Depression Inventory-II[2]

1. Goldman Consensus Group. The Goldman Consensus statement on depression in multiple sclerosis. *Multiple Sclerosis* 2005; **11**: 328-337
2. Crawford P, Webster NJ. Assessment of depression in multiple sclerosis: Validity of including somatic items on the Beck Depression Inventory-II. *Int J MS Care* 2009;11:167-173.

Clinical Characteristics

- Feeling sad or empty
- Irritable or crying most of the day
- Loss of energy
- Loss of interest or pleasure in most activities
- Significant change in appetite and weight
- Unusual sleep behavior
- Decreased sex drive
- Suicidal thoughts

Siegert RJ, Abernethy DA. *J Neurol Neurosurg Psychiatry*. 2005;76(4):469-475.
NMSS. http://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms/Depression.

Comprehensive Management

- Provide a supportive, therapeutic environment
- Identify risk factors (screening, self-report, environmental factors, family history)
- Combination psychotherapy and antidepressants
- Wellness focus (exercise)
- Be alert for suicidal ideation/plan
- Assess and reassess continually
- Adjust medications appropriately

Bashir et al. *Handbook of Multiple Sclerosis*. 2002.
Patten. *Int J MS Care* 2009;11:174-179.

Pharmacologic Treatment

SSRIs	Dose	Adverse Effect
Fluoxetine	20-80 mg/d	Nausea, insomnia, diminished libido
Sertraline	25-200 mg/d	Nausea, fatigue, diminished libido
Paroxetine	20-50 mg/d	Nausea, insomnia, diminished libido
Citalopram	20-40 mg/d	Nausea, somnolence, diminished libido
Escitalopram	10-20 mg/d	Nausea, insomnia, diminished libido
SNRIs	**Dose**	**Adverse Effect**
Venlafaxine	75-225 mg/d	Nausea, dizziness
Duloxetine	40-60 mg/d	Nausea, insomnia

SNRI=serotonin/norepinephrine reuptake inhibitor; SSRI=selective serotonin reuptake inhibitor

Schapiro. *Neurorehabil Neural Repair*. 2002;16(3):223-231.
Medline Plus Drug Information. http://www.nlm.nih.gov/medlineplus/druginformation.html.

Patient Resources

- Multiple Sclerosis Foundation. The many shadows of MS related depression. http://www.msfocus.org/article-details.aspx?articleID=413
- Multiple Sclerosis Foundation. Caring for your emotional health. http://www.msfocus.org/article-details.aspx?articleID=414
- National MS Society. Depression & multiple sclerosis. http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-Depression.pdf

CONCLUSION

Nursing Implications

- Many MS symptoms overlap
- Educate patients regarding role of contributing factors (i.e. medications, infections, heat, deconditioning, etc.)
- When a symptom is new or suddenly worsens, re-evaluate contributing factors including disease activity.

Nursing Implications

- Lifestyle matters! Reinforce importance of exercise, nutrition, stress management, smoking cessation, adequate sleep
- Gauge impact of symptom(s) on patients' lifestyle before recommending treatment
- Lifestyle modifications may be all that is needed/desired to address symptom(s)

Nursing Implications

- When possible, include family/loved ones in the discussion.
- Up to 80% information given at an office visit is forgotten as soon as a patient leaves the office.
- Provide more than one form of instruction, especially when cognitive impairment is suspected (verbal, written, handouts, website information)

QUESTION AND ANSWER SESSION

Thank you for your participation!

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- For upcoming *Caring for the Patient with MS* Webinars, please visit our web page at: http://www.iomsn.org/component/content/article/239

- For additional IOMSN educational opportunities and future webinar programs, please visit IOMSN at: www.IOMSN.org

- We look forward to seeing you for our next CNE webinars:
  - WEBINAR 6: Adherence on November 17, 2014
  - WEBINAR 7: Psychosocial Considerations in MS on January 26, 2015